WEST Search History

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DATE: Friday, October 20, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L11	l9 and L10	3
☐	L10	L8 and patients	16
☐	L9	L8 and isopeptidase	3
☐	L8	sumo and neurodegeneration	17
	DB=DWPI,JPAB,EPAB,USOC,USPT,PGPB; PLUR=YES; OP=ADJ		
☐	L7	THOMPSON-LESLIE-M!	5
☐	L6	THOMPSON-LESLIE-M!	5
☐	L5	MARSH-J-LAWRENCE!	11
☐	L2	STEFFAN-J-S!	3
☐	L1	STEFFAN-J-S!	3

END OF SEARCH HISTORY

Caseft 10/789,518
WEST (PGPB, USPT, USOC, EPAB, JPAB, DWPI).

AD
10/20/06

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FILE 'MEDLINE' ENTERED AT 13:16:11 ON 20 OCT 2006

FILE 'BIOSIS' ENTERED AT 13:16:11 ON 20 OCT 2006
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=> s polyglutamine and neurodegeneration
L1          556 POLYGLUTAMINE AND NEURODEGENERATION

=> s small ubiquitin-like modifier
L2          304 SMALL UBIQUITIN-LIKE MODIFIER

=> s l2 and isopeptidase
L3            7 L2 AND ISOPEPTIDASE

=> s l1 and l3
L4            0 L1 AND L3

=> s SUMO and ubiquitin
L5         1181 SUMO AND UBIQUITIN

=> s l5 and isopeptidase
L6           44 L5 AND ISOPEPTIDASE

=> s l1 and l6
L7            0 L1 AND L6

=> s ubiquitin and l1
L8           65 UBIQUITIN AND L1

=> s l8 and isopeptidase
L9            0 L8 AND ISOPEPTIDASE

=> s l8 and huntington
L10          32 L8 AND HUNTINGTON

=> s l10 and therapy
L11           4 L10 AND THERAPY

=> display l11 ibib abs 1-4

L11  ANSWER 1 OF 4     MEDLINE on STN
ACCESSION NUMBER:   2005390430     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 16048838
TITLE:              Role of molecular chaperones in neurodegenerative
                    disorders.
AUTHOR:             Meriin A B; Sherman M Y
CORPORATE SOURCE:   Department of Biochemistry, Boston University Medical
                    School, MA, USA.
SOURCE:             International journal of hyperthermia : the official
                    journal of European Society for Hyperthermic Oncology,
                    North American Hyperthermia Group, (2005 Aug) Vol. 21, No.
                    5, pp. 403-19.  Ref: 128
                    Journal code: 8508395. ISSN: 0265-6736.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200510
ENTRY DATE:         Entered STN: 29 Jul 2005
                    Last Updated on STN: 21 Oct 2005
                    Entered Medline: 20 Oct 2005
AB   Many major neurodegenerative diseases, including Amyotrophic Lateral
     Sclerosis, Alzheimer's disease, Parkinson's disease, Huntington
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Case # 10/789,518
STN (BIOSIS, MEDLINE)
10/20/06
AA

Disease and other polyglutamine expansion disorders, are associated with degeneration and death of specific neuronal populations due to accumulation of certain abnormal polypeptides. These misfolded species aggregate and form inclusion bodies and their neurotoxicity is associated with the aggregation. To handle a build-up of abnormal proteins cells employ a complicated machinery of molecular chaperones and various proteolytic systems. Chaperones facilitate refolding or degradation of misfolded polypeptides, prevent protein aggregation and play a role in formation of aggresome, a centrosome-associated body to which small cytoplasmic aggregates are transported. The ubiquitin -proteasome proteolytic system is critical for reducing the levels of soluble abnormal proteins, while autophagy plays the major role in clearing of cells from protein aggregates. Accumulation of the aggregation prone proteins activates signal transduction pathways that control cell death, including JNK pathway that controls viability of a cell in various models of Parkinson's and Huntington's diseases. The major chaperone Hsp72 can interfere with this signalling pathway, thus promoting survival. A very important consequence of a build-up and aggregation of misfolded proteins is impairment of the ubiquitin -proteasome degradation system and suppression of the heat shock response. Such an inhibition of the major cell defense systems may play a critical role in neurodegeneration. Here, it is suggested that these changes may reflect a senescence-like programme initiated by the aggregated abnormal polypeptides. Pathways that control the fate of misfolded proteins, for example molecular chaperones or proteolytic systems, may become interesting novel targets for therapy of neurodegenerative disorders.

L11 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2004506712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15474886
TITLE: Essential fatty acids in Huntington's disease.
AUTHOR: Das Undurti N; Vaddadi Krishna S
CORPORATE SOURCE: UND Life Sciences, Walpole, Massachusetts 02081, USA.. Undurti@hotmail.com
SOURCE: Nutrition (Burbank, Los Angeles County, Calif.), (2004 Oct) Vol. 20, No. 10, pp. 942-7. Ref: 54
Journal code: 8802712. ISSN: 0899-9007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 13 Oct 2004
Last Updated on STN: 9 Apr 2005
Entered Medline: 8 Apr 2005

AB Huntington's disease is an inherited neurodegenerative disorder due to a mutation in exon 1 of the Huntingtin gene that encodes a stretch of polyglutamine (polyQ) residues close to the N-terminus of the huntingtin protein. Aggregated polyQ residues are highly toxic to the neuronal cells when they enter the cell nucleus. The mechanisms by which aggregated polyQ induces neurodegeneration include the binding of abnormal huntingtin to cyclic adenosine monophosphate response element binding protein, which hampers its ability to turn on transcription of other genes; mutant huntingtin binding to the active site on the cyclic adenosine monophosphate response element binding protein, which is essential for its acetyltransferase activity and, hence, the drugs that inhibit histone deacetylase arrest polyQ-dependent neurodegeneration; and/or disrupting the ubiquitin -proteasome system. Transgenic R6/1 mice that incorporate a human genomic fragment containing promoter elements exon 1 and a portion of intron 2 of the huntingtin gene responsible for Huntington's disease develop late-onset neurologic deficits in a manner similar to the motor

abnormalities of Huntington's disease and show increased survival rates and decreased neurologic deficits when supplemented with essential fatty acids throughout life. A randomized, placebo-controlled, double-blind study has shown that highly unsaturated fatty acids are beneficial to patients with Huntington's disease. These results raise the possibility that unsaturated fatty acids may prevent or arrest polyQ aggregation, inhibit histone deacetylase, and/or activate the ubiquitin-proteasome system. In view of the encouraging results with essential fatty acids in Huntington's disease, it is proposed that their possible use in other neurodegenerative conditions need to be explored.

L11 ANSWER 3 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2001415094 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11464455
TITLE: Triplet repeat disease, with particular emphasis of spinal and bulbar muscular atrophy (SBMA).
AUTHOR: Sobue G
CORPORATE SOURCE: Department of Neurology, Nagoya University School of Medicine.
SOURCE: Rinsho shinkeigaku = Clinical neurology, (2000 Dec) Vol. 40, No. 12, pp. 1193-5.
Journal code: 0417466. ISSN: 0009-918X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (LECTURES)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 1 Oct 2001
Last Updated on STN: 1 Oct 2001
Entered Medline: 27 Sep 2001

AB Spinal and bulbar muscular atrophy (SBMA) is an X-linked neurodegenerative disease caused by the expansion of a CAG repeat in the first exon of the androgen receptor (AR) gene. To date, eight CAG-repeat diseases have been identified, including spinal and bulbar muscular atrophy (SBMA). Huntington's disease (HD), dentatorubralpallidoluysian atrophy (DRPLA) and five spinocerebellar ataxias (SCAs 1, 2, 3, 6, 7). These disorders likely share a common pathogenesis caused by the gain of a toxic function associated with the expanded polyglutamine tract. Several mechanisms have been postulated as a pathogenic process for neurodegeneration caused by the expanded polyglutamine tract. Processing of the polyglutamine containing proteins by proteases liberate truncated polyglutamine tract, which may cause neurodegeneration as demonstrated in transgenic mice and transfected cells. In addition to cellular toxicity, truncated and expanded polyglutamine tracts have been shown to form intranuclear inclusions (NI). The NIs formed by the disease protein are a common pathological feature of these diseases. In SBMA, NIs containing AR protein have been observed in regions of SBMA central nervous system susceptible to degenerations. Transcriptional factors or their cofactors, such as cerb or creb-binding protein (CBP) sequestrated in the NI may alter the major intracellular transcriptional signal transduction, and ultimately may result in neuronal degeneration. The ubiquitin -proteasome pathway may also contribute to the pathogenesis of CAG-repeat diseases. As for the therapeutic strategies, many possibilities have been demonstrated. Overexpression of Hsp70 and Hsp40 chaperones act together to protect a cultured neuronal cell model of SBMA from a cellular toxicity of expanded polyglutamine tract.

L11 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:438272 BIOSIS
DOCUMENT NUMBER: PREV200510222306
TITLE: Role of molecular chaperones in neurodegenerative disorders.

AUTHOR(S): Meriin, A. B.; Sherman, M. Y. [Reprint Author]
CORPORATE SOURCE: Boston Univ, Sch Med, Dept Biochem, Boston, MA 02118 USA
sherman@biochem.bmc.bu.edu
SOURCE: International Journal of Hyperthermia, (AUG 2005) Vol. 21, No. 5, pp. 403-419.
CODEN: IJHYEQ. ISSN: 0265-6736.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Oct 2005
Last Updated on STN: 26 Oct 2005

AB Many major neurodegenerative diseases, including Amyotrophic Lateral Sclerosis, Alzheimer's disease, Parkinson's disease, Huntington Disease and other polyglutamine expansion disorders, are associated with degeneration and death of specific neuronal populations due to accumulation of certain abnormal polypeptides. These misfolded species aggregate and form inclusion bodies and their neurotoxicity is associated with the aggregation. To handle a build- up of abnormal proteins cells employ a complicated machinery of molecular chaperones and various proteolytic systems. Chaperones facilitate refolding or degradation of misfolded polypeptides, prevent protein aggregation and play a role in formation of aggresome, a centrosome- associated body to which small cytoplasmic aggregates are transported. The ubiquitin - proteasome proteolytic system is critical for reducing the levels of soluble abnormal proteins, while autophagy plays the major role in clearing of cells from protein aggregates. Accumulation of the aggregation prone proteins activates signal transduction pathways that control cell death, including JNK pathway that controls viability of a cell in various models of Parkinson's and Huntington's diseases. The major chaperone Hsp72 can interfere with this signalling pathway, thus promoting survival. A very important consequence of a build- up and aggregation of misfolded proteins is impairment of the ubiquitin - proteasome degradation system and suppression of the heat shock response. Such an inhibition of the major cell defense systems may play a critical role in neurodegeneration. Here, it is suggested that these changes may reflect a senescence- like programme initiated by the aggregated abnormal polypeptides. Pathways that control the fate of misfolded proteins, for example molecular chaperones or proteolytic systems, may become interesting novel targets for therapy of neurodegenerative disorders.